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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,282	01/23/2004	Hassan Benameur	1759.051A	9192

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HESLIN ROTHENBERG FARLEY & MESITI PC
5 COLUMBIA CIRCLE
ALBANY, NY 12203

EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,282	BENAMEUR ET AL.	
	Examiner	Art Unit	
	Aradhana Sasan	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/23/2004, 03/17/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Claims 1-13 were cancelled.

2. Claims 14-24 were amended and new claims 24-28 were added.

3. Claims 14-28 are being presented for examination.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on July 27, 2001. It is noted, however, that applicant has not filed a certified copy of the application (FR01.10094) as required by 35 U.S.C. 119(b).

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 01/23/2004 and 03/17/2004 were filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner. See attached copy of PTO-1449.

Drawings

5. It is recommended that the heading "Brief Description of Drawings" precede the description of the drawings.

Claim Objections

6. Claim 14 objected to because after the composition of (ii) an "and" or "or" is missing. It is not clear if part (iii) is required or is optional. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 14 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a statin as a water insoluble active (page 4, lines 24-28), does not reasonably provide enablement for any active principle.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The scope of the claim is broad enough to encompass the use of any active principle, not just the use of statins such as simvastatin.

The specification provides guidance for using statins as active agents in the composition because "simvastatin undergoes a strong first intestinal passage effect" (page 1, lines 10-13).

Working examples provided are directed toward compositions comprising of simvastatin (page 4, examples 1-3).

The specification does not teach that any active principle can be used in the composition. The nature of the composition is such that the active principle would have to interact with the lipophilic/hydrophobic phase and not all active principles have this property.

The nature of the invention is a composition comprising (a) an active principle, (b) a self micro-emulsifying carrier comprising of (i) a lipophilic phase, (ii) a surfactant phase, (iii) a co-surfactant phase.

The state of the prior art teaches that simvastatin is a relatively hydrophobic compound (Mauro, page 197). Igel et al. teach that, "with the exception of pravastatin and rosuvastatin, all statins are lipophilic compounds (Igel et al., page 836). It is also taught that "all statins undergo hepatic metabolism via cytochrome P450 isoenzymes" and these isoenzymes "are the most abundant and account for approximately ... 80% in small intestinal mucosa" (Igel et al., page 838).

Undue experimentation would be required to use the invention because it is not clear which active principle is going to be used in the composition. In order to use any active principle with the invention, the quantity of experimentation would be too great.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim. It would require undue experimentation to use the invention based on the breadth of these claim.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 14-17, 24-25, and 27 rejected under 35 U.S.C. 103(a) as being unpatentable over Farah et al. (US 6,054,136).

Farah teaches a self-microemulsifying drug delivery system (Col 1, lines 10-19). The composition is for oral use and is capable of forming a microemulsion in situ with the biological fluid of the body and comprises a pharmaceutical active ingredient, a lipophilic phase, a surfactant, and a co-surfactant (Col 8, lines 39-43, Claim 1). The surfactant is "obtained by an alcoholysis reaction of polyethylene glycol and a fraction of oil ... consisting of caprylic and capric acids" (Col 8, Claim 1). The surfactant and co-surfactant ratio is 0.5 (Col 5, line 67). The surfactant has an HLB of less than 16 (Col 9, line 47). The lipophilic phase of the composition has an HLB of less than 16 (Col 8, lines 44-45 and lines 50-51).

Farah et al. do not teach the lipophilic phase of the composition being in the range 50%-95% by weight.

As to claim 15, Farah teaches the lipophilic phase of the composition being in the range 1%-75% by weight and having an HLB of less than 16 (Col 8, lines 44-45 and lines 50-51). The HLB of the lipophilic phase of the instant application is 14; therefore it is anticipated by Farah. Although the weight range of the lipophilic phase of the instant

application does not overlap the weight range disclosed in the reference, a person with ordinary skill in the art could, without absent evidence to the contrary, arrive at the optimal weight range without undue experimentation.

As to claims 16 and 17, Farah teaches that the surfactant-co-surfactant mixtures range from 18.5%-35% of the weight of the composition (Examples 1 and 3, Col 5, lines 22-24 and lines 65-67). Although the surfactant and co-surfactant levels of the instant application do not exactly overlap the combined surfactant-co-surfactant levels of the reference, a person with ordinary skill in the art could, without absent evidence to the contrary, arrive at the optimal weight levels without undue experimentation.

11. Claims 18-23 rejected under 35 U.S.C. 103(a) as being unpatentable over Farah et al. (US 6,054,136), and further in view of Lipari et al. (WO 00/37057).

Farah teaches a pharmaceutical composition for oral use that is capable of forming a microemulsion, and comprises a pharmaceutical active ingredient, a lipophilic phase, a surfactant, and a co-surfactant (Col 8, lines 39-43, Claim 1). Farah also teaches a method of increasing bioavailability of a pharmaceutical active ingredient which is difficult to dissolve. This method includes use of the said composition. Farah does not teach statins or simvastatin as the pharmaceutical active ingredient or the use of propylene glycol monocaprylate in the co-surfactant phase.

Lipari teaches "formulations for oral administration comprising lipid regulating agents having enhanced bioavailability" (Page 3). The formulation contains propylene glycol fatty acid esters that includes propylene glycol monocaprylate (Page 3, Page 5

Claims 5 and 6). Lipari also specifically teaches the use of a statin in the formulation (Page 5, Claim 4).

Thus, a person having ordinary skill in the art at the time the invention was made would have found it obvious to combine the pharmaceutical composition teaching of Farah with the statin formulation with propylene glycol monocaprylate taught by Lipari because of the improved bioavailability of the statin that would be conferred by the forming a microemulsion. Simvastatin is a known statin drug.

As to claims 22 and 23, a person with ordinary skill in the art could, without absent evidence to the contrary, arrive at the optimal weight of the active ingredient (simvastatin) in the composition without undue experimentation.

12. Claims 26 and 28 rejected under 35 U.S.C. 103(a) as being unpatentable over Farah et al. (US 6,054,136), Lipari et al. (WO 00/37057), and further in view of Patel et al. (US 6,248,363).

The teachings of Farah and Lipari are stated above. The emulsifying systems in these references do not specifically include lauric macrogolglycerides and caprylocapric macrogolglycerides.

Patel teaches that the bioavailability of simvastatin (Col 6, line 49) can be improved by their invention, which includes the surfactant lauric macrogolglycerides as the surfactant (Col 35, line 46, Col 65, lines 50-53, claim 16). The preferred surfactants include lauryl macrogolglycerides (Col 30, lines 45-47). The use of caprylic/capric glycerides is also disclosed (Col 17, Table 5).

Thus, a person having ordinary skill in the art at the time the invention was made would have found it obvious to combine the pharmaceutical composition teaching of Farah with the statin formulation with propylene glycol monocaprylate taught by Lipari and further combine it with the surfactants disclosed by Patel because these surfactants are known in the art to work in emulsifying systems for improving bioavailability of poorly soluble drugs (like statins).

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang or Cecilia Tsang, can be reached at 571-272-8011 and 571-272-0562 respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600